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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,101	12/10/2001	Thomas Schmulling	1195-2	2633

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,101	SCHMULLING ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/1/2004, 1/18/2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-138* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-17,25,28-44,46,47,49,50,52,53,79-81,86,87,90-92,95-101,103-121 and 138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,6,18-24,26,27,45,48,51,54-78,82-85,88,89,93,94,102 and 122-137.

DETAILED ACTION

1. The amendment filed 9/1/2004, the Oath and Declaration filed 9/14/2004, the Foreign Priority Document filed 11/19/2004 and the new CRF filed 1/18/2005 have all been entered.

2. Claims 1-138 are pending.

Claims 5-6, 18-24, 26-27, 45, 48, 51, 54-78, 82-85, 88-89, 93-94, 102, 122-137 have been withdrawn from consideration for being drawn to non-elected inventions.

3. Claims 1-4, 7-17, 25, 28-44, 46-47, 49-50, 52-53, 79-81, 86-87, 90-92, 95-101, 103-121 and 138 are examined in the present office action.

4. Rejections and objections not set forth below are withdrawn.

5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Specification

6. In response to the objection of embedded hyperlink and/or other form of browser-executable code, it is Applicants intent that the hyperlinks and/or other forms of browser-executable code be disabled (see page 23, 1st paragraph of response filed 9/1/2004).

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim has been amended to recite "GHs (SEQ ID NO:38), VGGTLSN (SEQ ID NO:39), VLGGLGOFG (SEQ ID NO:40), AND ITRARI (SEQ ID NO:41)". Applicants contend that the individual sequence motifs may be discerned from the sequence alignments in Figure 2 (page 27, 2nd paragraph of response). The Office contends that Applicants have selected an arbitrary group of amino acids and have not selected or claimed all conserved amino acids. Applicants are required to point to support for "GHs (SEQ ID NO:38), VGGTLSN (SEQ ID NO:39), VLGGLGOFG (SEQ ID NO:40), AND ITRARI (SEQ ID NO:41)" or to amend the claims to delete the NEW MATTER.

Written Description

8. Claims 1-4, 7-17, 25, 28-44, 46-47, 49-50, 52-53, 79-81, 86-87, 90-92, 95-101 and 103-121 remain rejected and claim 138 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 6/2/2004. Applicant's arguments filed 9/1/2004 have been fully considered but they are not persuasive.

Applicants contend that CKX is an FAD binding enzyme and that at the time of filing CKX was known to contain an FAD binding domain (page 27, 2nd paragraph). Applicants contend that Houba-Herin et al (1999, Plant Journal 17:615-626) teach that a conserved GHS motif exists as a putative FAD-binding site of many flavoprotein oxidoreductases. Applicants state from Houba-Herin et al "the deduced CKO amino acid sequence shows sequence similarity with a FAD binding domain, found in several oxidases" (page 27, bottom paragraph).

Applicants contend that amended claim 1 recites the GHS (SEQ ID NO:38) motif as well as sequence motifs found in the FAD binding domain described by Houba-Herin etal in the vicinity of amino acid residues 170-240 of Houba-Herin et al., i.e., VGGTLSN (SEQ ID NO:39), VLGGLGQFC (SEQ ID NO:40), and ITRARI (SEQ ID NO:41) (page 28, top paragraph).

The Office contends that not all oxidases are cytokinin oxidases and that the cytokinin oxidase cloned by Houba-Herin et al has a FAD binding site that shows similarity to the FAD binding site of other flavoproteins (see page 621, right column, 2nd paragraph). The claimed sequence i.e., SEQ ID NO:38 is not specific to cytokinin oxidases, but rather, is found in other enzymes that are characterized as having a FAD binding domain. In regards to SEQ ID NO:39, 40 and 41, Applicants have not provided a function for said sequences and have only stated that said sequences are located in the vicinity of the GHS sequence.

Applicants contend that claim 1 meets the written description requirement because the application discloses and claim 1 recites sufficiently detailed, relevant identifying characteristics, i.e., partial structure and functional characteristics (page 28, 2nd paragraph). Applicants contend that the specification is replete with written description of sequences falling within Applicants' invention as presently claimed, and points to pages 18-23 and 36-51 of the specification (page

28, bottom paragraph). Applicants contend that the application discloses SEQ ID NO:26 as well as an 84 bp fragment corresponding to nucleotides 1171-1254 of the AtCKX2 cDNA as set forth in SEQ ID NO:31. Applicants again point to pages 18-23 and 36-51 as providing written description support for claims 2 and 3 (paragraph bridging pages 29-30).

The Office contends that for claims drawn to SEQ ID NO:26 and SEQ ID NO:31, Applicants have fulfilled the written description requirement. The office contends that the disclosure on pages 18-23 and 36-51 of the specification does not provide written description support for claims drawn to degenerated nucleic acid molecules, nucleic acid molecules which are divergent, or which are divergent due to differences between alleles, or functional fragments, or nucleic acid molecule that hybridizes under medium stringency, or nucleic acid molecules encoding a protein exhibiting 70% similarity to SEQ ID NO:4, or nucleic acid molecules encoding an immunologically active fragment of a cytokinin oxidase, or functional fragment of a cytokinin oxidase. The disclosure on pages 18-23 and 36-51 does not provide additional sequences that have been exemplified but rather the disclosure recites claim limitations and definitions.

Applicants contend that Figure 2 provides an alignment of different cytokinin oxidases where the known signature sequences, such as those presently presented in claim 1, are clearly visible (page 30 bottom paragraph).

The office contends that the amino acid sequences presented in Figure 2 are for four CKX proteins isolated from Arabidopsis and one CKX sequence from maize. Applicants have not presented a representative number of sequences from all plants, which include gymnosperms and basal dicots, e.g., water lilies. In addition, the office appreciates the relevance of amino

acids that are conserved between protein homologues from different plant species, but, the burden is for Applicant to describe the functional domains of the protein that are essential for the protein to function. This includes general domain, e.g., a FAD binding domain, and domains that are specific to the genus which Applicants are claiming as their invention.

Scope of Enablement

9. Claims 1-4, 7-17, 25, 28-44, 46-47, 49-50, 52-53, 79-81, 86-87, 90-92, 95-101 and 103-121 remain rejected and claim 138 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for stimulating root growth, enhancing lateral or adventitious root formation, increasing seed size, increasing root growth, delay senescence, increase leaf thickness, decrease vessel size, increase branching and effecting the expression of a polypeptide encoded by SEQ ID NO:26 and increasing the size of the root meristem, comprising transforming a plant with a nucleic acid sequence comprising SEQ ID NO:26 encoding SEQ ID NO:4, and vector, host cells, plant cells and plants transformed therewith, does not reasonably provide enablement for methods for stimulating root growth or enhancing lateral root formation comprising nucleic acids hybridizing to SEQ ID NO:26, nucleic acids that are diverging from a nucleic acid encoding SEQ ID NO:4, nucleic acids diverging from those nucleic acids as specified in claim 2 due to differences between alleles, functional fragments of said nucleic acids having biological activity of a cytokinin oxidase, a nucleic acid encoding an amino acid sequence comprising SEQ ID NO:32 and which is at least 70% similar to the amino acid sequence of SEQ ID NO:4, a nucleic acid encoding any immunologically active fragment of a cytokinin oxidase encoded by SEQ ID NO:26 or any immunologically active fragment encoded

by any of the nucleic acids specified in claim 3, a nucleic acid encoding any functional fragment of any cytokinin oxidase encoded by SEQ ID NO:26 or any previously mentioned sequence. In addition, Applicants' disclosure does not reasonably provide enablement for methods for altering root geotropism, increasing yield, altering leaf senescence, and improving standability of seedlings, comprising transforming a plant with SEQ ID NO:26 encoding SEQ ID NO:4 or any nucleic acid encoding a fragment of SEQ ID NO:4 or a immunologically active fragment, or nucleic acid encoding a divergent polypeptide or a nucleic acid that hybridizes with SEQ ID NO:26, or any of the nucleic acids listed in claim 2 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 6/2/2004. Applicant's arguments filed 9/1/2004 have been fully considered but they are not persuasive.

Applicants contend that the specification enables method for stimulating root growth, enhancing lateral root formation and effecting the expression of cytokine oxidase polypeptides using nucleotide sequences encoding cytokinin oxidases having as little as between 35% and 66% amino acid sequence similarity to each other. Given that, Applicants contend that the same methods are enabled using the claimed nucleic acids as recited in claims 2 and 3 (paragraph bridging pages 35-36).

The Office contends that Applicants have not provided guidance for determining which sequences that hybridize to SEQ ID NO:26, or which nucleic acid that are divergent from nucleic acid molecules encoding SEQ ID NO:4, or which nucleic acid molecules divergent from nucleic acid molecules recited in claim 2 due to differences in alleles, functional fragments of such

nucleic acid molecules having cytokine oxidase activity, or which nucleic acid molecules encoding an amino acid sequence comprising SEQ ID NO:32 and which is at least 70% similar to the amino acid sequence of SEQ ID NO:4, or which nucleic acid molecules encoding an immunologically active fragment of a cytokinin oxidase encoded by SEQ ID NO:26 or which immunologically active fragment encoded by any nucleic acids specified in claim 3, or which nucleic acid molecules encoding a functional fragment of a cytokinin oxidase can be used in the claimed invention. Absent any guidance, undue trial and error experimentation would be required by one skilled in the art to determine which nucleic acids are operable in the claimed invention.

Applicants contend that the Kaminek et al and Hare et al references relied upon by the examiner to demonstrate unpredictability are irrelevant to the presently claimed invention. Applicants contend that the claims recite a plant cytokinin oxidase with particular chemical structures and that cytokinin oxidases from different Phaseolus species have different enzyme activities are not relevant to the presently claimed invention (paragraph bridging pages 36 and 37).

The office contends that the Kaminek et al and Hare et al references demonstrate that not all cytokinin oxidases from plants are the same given that Applicants' claims are drawn to all cytokinin oxidases from plants. Given the different pH optimum for different cytokinin oxidases isolated from different species of Phaseolus, undue trial and error experimentation would be required by one of skill in the art to use Applicants' claimed invention.

Applicants contend that the claims do not require that the claimed cytokinin oxidases have the same activity as the protein encoded by SEQ ID NO:26. Applicants contend that what

is required is that the presently claimed nucleotide sequences encode a protein having cytokinin oxidase activity and that the molecules encoding such a protein work in the presently claimed methods (page 37, 1st full paragraph).

The Office contends that Applicants are claiming products and methods comprising nucleic acid molecules encoding a plant cytokinin oxidase. The Office does not understand Applicants'H assertion that the claims are directed to nucleotide sequences that encode a protein having cytokinin oxidase activity, rather than to nucleic acids encoding a protein having the same activitiy as the protein encoded by SEQ ID NO:26. The Office understands that the protein encoded by SEQ ID NO:26 is a cytokinin oxidase which inherently has cytokinin oxidase activity. Therefore, it appears a requirement of the claimed invention that the claimed nucleic acids have the same activity as the protein encoded by SEQ ID NO:26.

Applicants contend that Bowie et al do teach that proteins are tolerant of amino acid substitutions (page 38, 2nd paragraph).

The Office contends that even though Bowie et al do teach that some proteins are tolerant of amino acid substitutions, the article does teach that not all proteins are tolerant of amino acid substitutions and therefore, undue trial and error experimentation would be required by one skilled in the art to make and use the claimed invention.

Applicants contend that the information provided in Figure 2, which clearly indicates regions of amino acid identities and similarities between maize and Arabidopsis CKX1, has not been considered by the Examiner (page 39, 1st full paragraph). In addition, Applicants have provided a Table on pages 36-37 listing amino acids having similar properties (page 39, 2nd paragraph).

The Office contends that the information presented in Figure 2 was considered. The Office contends that Applicants' Figure 2 discloses four protein sequences, three from Arabidopsis and one from maize. Applicants have not presented a representative number of sequences from a representative number of plants. Absent the additional information, undue trial and error experimentation would be required by one skilled in the art to determine which amino acids can be altered and which amino acids are required.

Applicants question the relevance of the McConnell et al reference in regards to plant cytokinin oxidase expression (page 39, bottom paragraph).

The Office contends that the McConnell et al reference was cited as the state-of-the-art for teaching the unexpected outcome of altering essential amino acids within a protein.

Applicants contend that they fail to see the relevance of the Fourgox-Nicol et al reference and further contend that one skilled in the art could perform a hybridization experiment and determine if a nucleic acid molecule isolated by hybridization reactions encodes a claimed cytokinin oxidase (page 40, top paragraph).

The Office contends that the Fourgox-Nicol et al reference teaches unexpected results using hybridization technologies, even when the hybridization conditions are highly stringent.

Applicants contend that a method for altering root geotropism is enabled and that one skilled in the art would understand root geotropism to mean the downward growth of roots, which results in longer primary roots and/or lateral or secondary roots; including references to specific locations in the specification (page 42, bottom paragraph).

The Office contends that altering root geotropism is not enabled because Applicants have not demonstrated that the claimed method can alter the roots ability to sense gravity. The

meaning of root geotropism is the plants ability to sense or not sense gravity. Growing long roots is not a function of root geotropism, but rather is a function of growth and development.

Applicants contend that methods for increased yield are enabled and provides support in the specification. In addition, Applicants contend increased yield can be exemplified as increased biomass of one or more organs (page 43, 1st full paragraph).

The Office contends that Applicants define yield to also encompass an increase in seed number (see page 1, line 13 of specification). Applicants are not enabled for an increase in yield because Applicants disclose "Total number of seeds is lowered in AtCKX1 and AtCKX3 expressers" (page 119, lines 29-30).

Applicants contend methods for increased shoot growth is enabled and provide support in the specification (page 43, 3rd full paragraph).

The Office contends that increased shoot growth is not enabled because Applicants disclose "Interestingly, the WT scions grafted on the transgenic rootstocks looked healthier and were better developed" (page 117, lines 11-12). Applicants make no mention that plants transformed with Applicants' claimed invention exhibited increased shoot mass or weight or biomass. The Office does not consider the recitation "looked healthier" to mean that the plant exhibits an increase in growth compared to a control plant.

Applicants contend methods for improving standability of seedlings is enabled and provide support in the specification (page 44, 3rd paragraph). Applicants contend methods of improving lodging and early vigor is enabled and provide support in the specification (page 44, 5th and 6th paragraphs).

The Office contends that improving standability is not enabled. Applicants define improved standability to be equated with an increase in root growth. The Office contends that improved standability, and lodging is attributed to not only a healthy root system, but also a healthy and strong stem and branch system. Applicants have not disclosed that plants expressing a claimed nucleic acid exhibit an improved standability and lodging compared to plants not transformed with said nucleic acid. Applicants have only reported that plants transformed with the claimed nucleic acids have longer roots.

Applicants contend methods of increasing stress tolerance is enabled and provide support in the specification (page 45, 1st full paragraph).

The Office contends that Applicants have not disclosed transgenic plants expressing the claimed nucleic acids have an increase in stress tolerance compared to control plants. Applicants have only referenced prophetic examples in the specification purporting to increase stress tolerance and a table disclosing promoters. See for example page 64, table; page 70, lines 25-27.

35 USC § 102

10. Claims 1-4, 7-17, 25, 28-44, 49-50, 52-53, 87 and 98-101 remain rejected and claim 138 is rejected under 35 U.S.C. 102(b) as being anticipated by Morris (February, 1999, WO 99/06571). This rejection is maintained for the reasons of record set forth in the Official action mailed 6/2/2004. Applicant's arguments filed 9/1/2004 have been fully considered but they are not persuasive.

Applicants contend that the nucleic acid of Morris would not hybridize with SEQ ID NO:26 given the recited hybridization conditions for medium stringency conditions as recited in amended claims 2 and 3. Applicants present the calculation of the Tm for nucleic acids of various lengths and conclude that the maize CKX taught by Morris would not hybridize given the medium hybridization conditions recited in the amended claims (page 46, 1st full paragraph to page 47, 2nd full paragraph).

The Office contends that Morris teaches a nucleic acid encoding an immunologically active fragment of a cytokinin oxidase, or a nucleic acid encoding a fragment of a cytokinin oxidase and as such anticipates the claimed invention. In regards to the calculated Tm, as is known in the art, the Tm is for an ideal situation and most hybridization reaction temperatures are established empirically. The Office maintains that the nucleic acid disclosed by Morris would hybridize with Applicants claimed sequence under medium stringency conditions.

Applicants contend that Morris does not teach a method for producing a plant having enhanced root growth, or a plant having enhanced primary, lateral or adventitious root growth (page 47, 3rd full paragraph). Applicants contend that the prior art reference does not disclose every element of the claims (page 47, bottom paragraph).

The Office contends that the plants of Morris disclose all elements of Applicants' claimed invention. See *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC SCalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then the prior art anticipates the claimed method.

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
March 29, 2005

AMY J. NELSON, PH.D
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